



Ambler, G. K., Kotta, P. A., Zielinski, L., Kalyanasundaram, A., Ali, A., Chowdhury, M. M., & Coughlin, P. A. (2020). The effect of frailty on long-term outcomes in vascular surgical patients. *European Journal of Vascular and Endovascular Surgery*, 60(2), 264-272.  
<https://doi.org/10.1016/j.ejvs.2020.04.009>

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[10.1016/j.ejvs.2020.04.009](https://doi.org/10.1016/j.ejvs.2020.04.009)

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**Full title:** The effect of frailty on long-term outcomes in vascular surgical patients.

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**Manuscript body word count:** 4331

**Mini Abstract word count:** 40

**Structured Abstract word count:** 299

**Funding Sources:** GKA was supported by the NIHR Biomedical Research Centre at University Hospitals Bristol NHS Foundation Trust and the University of Bristol for part of the time that this research was carried out.

**Short title:** Long term effects of frailty in surgical patients

## What this study adds

Vascular surgery patients are predominantly elderly, often have significant comorbidity and are more likely to be frail. This study highlights that increasing severity of frailty in a cohort of vascular surgery patients is associated with poor outcomes at 5 years.

## Structured Abstract

**Objective:** Frailty is a multi-dimensional vulnerability due to age-associated decline.

We assessed the impact of frailty on long-term outcomes in a cohort of vascular surgical patients.

**Methods:** Patients aged over 65 years with length of stay (LOS) > 2 days admitted to a tertiary vascular unit over a single calendar year were included. Demographics, mode of admission, diagnosis were recorded alongside a variety of frailty-specific characteristics. Using the previously developed Addenbrookes Vascular Frailty Score (AVFS – 6 point score: anaemia on admission, lack of independent mobility, polypharmacy, Waterlow score > 13, depression and emergency admission) we assessed the effect of frailty on 5-year mortality and readmission rates using multivariate regression techniques. We further refined the AVFS to assess longer term outcomes.

**Results:** In total, 410 patients (median age 77 years) were included and followed up until death or five years since the index admission. One hundred and thirty-four were treated for aortic aneurysm, 75 and 96 for acute and chronic limb ischaemia respectively, 52 for carotid disease and 53 for other pathologies. The in-hospital mortality rate was 3.6%. The 1-, 3- and 5-year survival rates were 83%, 70% and 59% ; and the 1-, 3- and 5-year readmission-free survival rates were 47%, 29% and 22%

respectively. Independent predictors of 5-year mortality were age, lack of independent mobility, high Charlson score, polypharmacy, evidence of malnutrition and emergency admission ( $P<0.01$  for all).

Patients with AVFS 0 or 1 had restricted mean survival times which were 1 year longer than those with AVFS 2 or 3 ( $P<0.0001$ ), who in turn had restricted mean survival times over 1 year longer than those with AVFS of 4 or more ( $P<0.0001$ ).

**Conclusions:** Frailty factors are strong predictors of long-term outcomes in vascular surgery. Further prospective studies are warranted to investigate its utility in clinical decision-making.

**Key words:** Frailty, vascular surgery, mortality, readmission.

## Introduction

The population throughout the Western world is aging and will continue to do so through the first half of the twenty-first century<sup>1</sup>. It is estimated that the proportion of the population aged over 60 will reach 33% by the year 2050.<sup>1,2</sup>

As people age, their burden of chronic disease inevitably increases, leaving them with less physiological reserve to overcome the acute physiological stress encountered following surgical intervention. Yet advances in both surgical and anaesthetic practice mean that the physiological impact of surgery is reduced. For example, procedures that were historically contemplated in only fitter patients (eg. abdominal aortic aneurysm (AAA) repair), can now be undertaken in older patients with significantly increased comorbidity<sup>3</sup>.

The concept of frailty, defined by some as a multi-dimensional vulnerability due to age-associated decline in physiological reserve, is therefore of increasing interest to surgeons<sup>4,5</sup> and specifically vascular surgery, with around 60% of vascular surgical patients older than 65<sup>6-8</sup>. There is increasing evidence of the deleterious effect of frailty specific factors on short term outcomes yet the advent of minimally invasive interventions and an improvement in the management of allied chronic comorbidities means that older vascular surgery patients increasingly have a longer life expectancy<sup>9</sup>.

It is therefore timely to start to focus on the longer-term effects of frailty and to try and identify patient subgroups who have continuing poorer health outcomes. Given that the concept of frailty and its role in outcomes in surgical cohorts is still somewhat new there is a lack of robust data on the longer-term consequences of frailty characteristics across the surgical subspecialties. Such data would allow for better allocation of resources to the neediest, highlighted by recent review of vascular services across the UK. We have already published results on a vascular specific

frailty score – the Addenbrookes Vascular Frailty Score (AVFS) – which showed strong predictive power for outcomes including 1-year mortality rates, discharge to a care institution and prolonged length of stay<sup>9</sup>.

As such, the aim of this current study was to determine the predictive effect of the AVFS to assess longer term (5 year) outcomes in the same cohort of vascular surgical patients that have been previously followed up for only one year. Secondly, we were interested in determining whether other frailty specific characteristics were more predictive of poorer outcomes. With this in mind, we measured a large number of frailty relevant characteristics and used statistical techniques to select the best predictors. The primary outcome measure was mortality at five years from the start of the index admission. Secondary outcomes were total readmission rates and readmission-free survival.

## Methods

### Patients

All patients admitted to the Cambridge Vascular Unit during the period 1<sup>st</sup> January 2012 to 31<sup>st</sup> December 2012 were screened for inclusion in the study. The inclusion criteria were patients aged  $\geq 65$  years and those with a length of stay  $\geq 2$  days. These were chosen pragmatically in order to focus attention on a subset of patients who were more likely to suffer a degree of frailty, admitted with conditions that were more likely to be associated with a significant risk of adverse outcomes. A full description of initial data collection has previously been published<sup>9</sup>.

Patient demographics, mode of admission (elective or emergency, which was defined as an unplanned admission either from an outpatient clinic, through the emergency department or an interhospital transfer), diagnosis and management were recorded, along with frailty-specific characteristics. These frailty specific characteristics are recorded and defined where appropriate in Table 1<sup>4</sup>. Need for readmission and survival were determined for the 5-year period from the date of the index admission. Vascular services are delivered using a “hub and spoke” model within our vascular surgery network with all vascular surgery in-patient admissions occurring at the hub hospital. In order to accurately capture re-admissions, the electronic hospital records at all spoke hospitals were interrogated specifically for all readmissions over a 5-year period following the index admission.

### Addenbrookes Vascular Frailty Score

Frailty was determined by scoring all patients using the Addenbrookes Vascular Frailty Score (AVFS) based upon the clinical assessment on the day of admission.



The AVFS is a 6 point score based on the following variables - anaemia on admission (Haemoglobin less than 120 g/L), lack of independent mobility, polypharmacy (defined as more than eight regular medications), a Waterlow score greater than 13, a history of depression and an emergency admission. This score has been previously shown to be predictive of one-year mortality in this cohort of vascular surgery patients<sup>9</sup>.

### Statistical analysis

The impacts of frailty on survival and readmissions were investigated using both univariate and multivariate regression modelling for all quantities of interest. Data on short-term outcomes (prolonged LOS, discharge destination, and inpatient healthcare-related cost) have previously been reported.<sup>9</sup> P-values for univariate analysis were corrected for multiple testing using the Bonferroni-Holm method<sup>10</sup>. Optimal multivariate models were developed by performing stepwise minimisation of Akaike's Information Criterion<sup>11</sup> and fine-tuned by then removing terms with Wald P-values greater than 0.1.

For survival and readmission-free survival, univariate P-values were calculated using the log-rank test, while multivariate analysis made use of Cox regression analysis<sup>12</sup>. Receiver operating characteristic curve analysis<sup>13,14</sup> was used to assess the ability of frailty scores to predict 5-year survival and readmission-free survival, and bootstrapping with 2000 replicates was used to estimate confidence intervals and compare the discrimination of different frailty scores. The ability of frailty scores to divide patients into low, intermediate and high-risk groups according to restricted mean survival time over the five-year follow-up period was also assessed.

Analysis was performed using the R statistical software version 3.5.1 (The R Foundation for Statistical Computing, <http://www.r-project.org/foundation>)<sup>15</sup> together with the ‘survival’<sup>16</sup>, ‘pROC’<sup>17</sup> and ‘survRM2’ packages<sup>18</sup>.

## Results

There were nine-hundred and forty-seven admissions to the Vascular Unit between 1<sup>st</sup> January 2012 and 31<sup>st</sup> December 2012, involving 823 patients. Five-hundred and sixty-one patients were more than 65 years old on their first admission to the unit, of whom four-hundred and thirteen patients had a length of stay greater than or equal to 2 days, and therefore met both of the inclusion criteria (Figure 1). The median age of this reduced cohort was 77 (range 65 – 95) years. Data was incomplete for three patients, so these were excluded from the analysis. Weight, BMI and serum albumin were not available for a significant number of patients and so were excluded from the multivariate analysis, but data on the remaining parameters was available for each patient.

Out of 410 patients analysed on the day of the index admission, 60 had an AVFS score of zero, 104 had a score of one, 93 had a score of two, 74 had a score of three, 54 had a score of four, and 24 had a score of five. Only one patient had a frailty score of six.

## Mortality

All patients were followed up to time of death or to 5 years post index admission. The in-hospital mortality rate was 3.6% during the index admission. Survival rates at 1, 3 and 5 years were 83%, 70% and 59%, respectively. A number of the frailty specific characteristics that were assessed (Table 1) were significantly associated with long-term patient survival at 5 years (Table 2). Multivariate analysis of all the frailty specific characteristics revealed that six factors - patient age, lack of independent mobility, high Charlson comorbidity index, polypharmacy, evidence of malnutrition

and emergency admission - were independent predictors of poor survival (Table 2). These six factors were combined to form a new frailty score specific for longer term outcomes – the Longer term Addenbrookes Vascular Frailty Score (LAVFS), with 1 point for each of the six factors.

We then compared the AVFS and LAVFS with specific to 5-year mortality rates. The AVFS remained a good tool for stratifying patients according to their long-term survival (C-statistic 0.756 at 5-years, 95% C.I. 0.709–0.802; Figure 2). Patients with AVFS 0 or 1 had restricted mean survival times which were 1 year longer than those with AVFS 2 or 3 (mean difference 12.1 months, 95% C.I. 8.2—16.1 months,  $P<0.0001$ ), who in turn had restricted mean survival times over 1 year longer than those with AVFS of 4 or more (mean difference 17.1 months, 95% C.I. 10.8—23.3 months,  $P<0.0001$ ).

The LAVFS identified as significant independent predictors of long-term survival shown in table 2 also stratified patients well into groups (Figure 2b) and had improved discrimination when predicting long-term survival when compared to the AVFS (C-statistic 0.789 at 5-years, 95% C.I. 0.764–0.832,  $P=0.028$  for improved discrimination over the AVFS - Figure 3). The LAVFS also divided patients into distinct survival groups. Patients with LAVFS 0 or 1 had restricted mean survival times which were almost 1 year longer than those with AVFS 2 or 3 (mean survival difference 10.7 months, 95% C.I. 6.8—14.6 months,  $P<0.0001$ ), who in turn had restricted mean survival times over 1 year longer than those with LAVFS of 4 or more (mean survival difference 17.2 months, 95% C.I. 11.2—23.1 months,  $P<0.0001$ ).

## Readmissions

Over the five years following the index admission, the majority (70%) of patients were readmitted, often multiple times. The median number of readmissions was 2 (IQR 0–4), with one patient re-admitted 23 times. In total, the 410 patients were readmitted for 9665 days during the five years following their index admission (approximately 24 days per patient). Slightly more than half of these were in the vascular hub (5411 days), with a smaller proportion in spoke hospitals (4254 days). Of the 298 patients for whom the hub was not their local hospital, 4209 admission days were in the spoke hospital, with only 1989 days in the Vascular hub (32%), with 180 (60%) patients not readmitted to the hub within 5 years of their index admission. The vast majority (8078; 84%) of readmission days were associated with unplanned readmissions.

## Readmission-free survival

At 1-, 3- and 5-years, the readmission-free survival was 48%, 28% and 21% respectively. Frailty characteristics were again associated with poor readmission-free survival (Table 3). Multivariate analysis revealed that advanced age, poor mobility, multiple comorbidities, polypharmacy, emergency admission and having had a limb-related admission were independent predictors of readmission or death (Table 3). The AVFS was a good discriminator of re-admission-free survival in the 5-year follow-up period (C-statistic 0.66, 95% C.I. 0.59-0.72), stratifying patients well into different risk groups (Figure 4). The LAVFS had similar discrimination (C-statistic 0.69, 95% C.I. 0.63-0.75,  $P=0.131$  for improved discrimination over the AVFS). The AVFS divided patients into distinct low, intermediate and high risk groups with respect to restricted mean readmission-free survival time, with low-risk patients (score 0 or 1) having readmission-free survival times on average 10.5 months (95%

C.I. 5.5—15.4 months) longer than intermediate-risk patients (scores 2 or 3), which were on average 9.5 months (95% C.I. 4.6—14.3 months) longer than high-risk patients (score 4 or more). Results were similar for the LAVFS.

## Discussion

This study is the first to look at the longer-term effects of frailty in a group of vascular surgery patient. It confirms that increasing degrees of frailty predict longer term patient relevant outcomes, namely risk of death and readmission free survival, in a cohort of vascular surgery inpatients. Further, this study shows that the AVFS continues to be a strong predictor of poor patient outcomes out to 5 years.

Continuing improvements in the management of both acute medical emergencies and chronic diseases has naturally resulted in patients living longer but at the cost of increasing numbers of patients with an increasing plurality of significant comorbidities. This is very pertinent to vascular surgery patients. Further, such aging of the population has also resulted in an increase in the prevalence of both mental and physical impairment, including both dementia and frailty<sup>19</sup>.

Advances in technology have meant however, that we have an increasing repertoire of minimally invasive techniques to treat vascular conditions. Given this, as vascular surgeons we increasingly face challenges in clinical decision making in this specific demographic group of patients. As such, it is essential to reliably stratify the outcomes of such elderly and frail patients.

Our previous publication showed that frailty, defined as a multifactorial medical syndrome characterised by reduced physiologic function and increased vulnerability for dependency and death, predicted a multiplicity of poor outcomes including

mortality, length of stay and discharge destination all out to one year<sup>9</sup>. Such findings are also replicated across a number of other medical and surgical specialities. Yet, the vast majority of published surgical studies on frailty focus on short term effects predominantly out to one year<sup>20-1</sup>. By comparison, few studies have looked at the effect of frailty on longer term outcomes in surgical patients. Two studies have reported 5-year mortality rates in older surgical patients following kidney transplant and patients treated for colorectal cancer and Makhani *et al* reported on 4-year survival in a cohort of frail patients predominantly undergoing urological procedures<sup>22-24</sup>. All of these studies showed that frailty continues to have a significant impact on mortality with regard to mid- and longer-term outcomes. This study offers a slightly different perspective in that it includes a cohort of patients admitted to the vascular surgery department including patients undergoing operative (open and endovascular) and non-operative intervention.

Increasing frailty predicts longer term mortality in our mixed cohort of vascular surgery patients with a 5-year mortality rate of 59% – worse than a number of common malignancies. Our previously developed AVFS continues to be a strong predictor of mortality. It effectively divides patients into high, intermediate and low risk groups, with patients in a lower risk group surviving on average over a year longer than those in a higher group. It also continues to provide focus on potential reversible factors – anaemia, poor mobility, polypharmacy, depression and nutrition. Reworking the analysis focusing purely on 5-year mortality provides us with a slightly different scoring system – namely the LAVFS. Within this, there are a number of common factors from both scores (emergency admission, polypharmacy, mobility, nutrition) with the main difference between the scores being the significance of age and the Charlson score, a marker of comorbidity, in the LAVFS. This is

perhaps unsurprising when one considers more longer-term outcomes but continues to highlight the potential benefits here of early involvement of specialists with an interest in frailty, namely medicine for the elderly physicians.

Not only would such intervention potentially reduce the mortality risk but it is also likely to reduce the risk of readmission. There is an increasing recognition of the role of geriatricians in the management of surgical patients. This is probably best delivered using the concept of comprehensive geriatric assessment (CGA), a multidimensional holistic assessment of an older person which considers health and wellbeing and ultimately leads to the formulation of a plan to manage issues of concern to the older patient and where relevant their family and caregivers.

The positive effect of CGA is evident in patients admitted for elective vascular surgery and has been shown to result in a shorter length of stay, lower incidence of complications and less likelihood of discharge to a higher level of dependency<sup>25</sup>.

No data yet exists looking at the effect of comprehensive geriatric assessment in non-elective admissions, yet it is likely that the positive effect will be even greater than that seen in the elective setting although whether CGA at an index admission would have long term effects would need further investigation. It would be valuable to see the effect of a community geriatrics / frailty team which would provide focused frailty specific interventions and as such the AVFS could identify the “at risk” cohort. This would link in with the longer term aim of delivering more care within the community and there is no doubt that more community based vascular care could dovetail well with this sort of community frailty team. As the population ages this will become more pressing to prevent unnecessary admissions to hospital.

This study also emphasises the significant comorbidity seen in vascular surgery patients reflected in the high frequency of readmissions. Seventy percent of patients



were readmitted over the 5-year follow-up period, equating to a total of 9665 days or 24 days per patient, with the majority of these being unplanned admissions. The high rate of readmissions in vascular surgery patients has been highlighted in the recent Getting It Right First Time (GIRFT) report for vascular surgery published in the UK last year <sup>26</sup>. GIRFT is part of a nationally driven deep dive of all medical and surgical specialties in each hospital within the UK to identify areas of good practice and areas for improvement. A key recommendation from this report focused on working to reduce avoidable readmissions by improving perioperative care and follow up including close liaison with medical specialties and early engagement with patients post-operatively. While this report focused primarily on the early period post discharge, the results from this study would further highlight the potential need for such early engagement with this cohort of patients which may provide benefit for patients in the longer term.

The GIRFT report also reflects on the possible benefits for continued centralisation of vascular services to create a critical mass of surgeons in the hub hospital allowing provision of a more comprehensive service to patients. This is acutely pertinent to the provision of vascular surgery services within the UK but may also reflect models of care in other countries.

Unlike other frailty scores, the AVFS is specific for a vascular surgery cohort and can be calculated based on the admission medical and nursing assessments. There a number of more generic frailty scores including the Clinical Frailty Scale (CFS) of the Canadian Study on Health & Aging. The fact that there are numerous frailty scores available highlights the complexity around the true definition of frailty and that frailty may represent variable issues in different disease groups. Indeed, the fact that there is a large number of frailty scores available suggests there is currently not one tools that

fits all. The AVFS (LAVFS) is the first vascular specific tool developed yet it is likely that when we analysis patient cohorts that a combination of both a generic frailty score and a more disease specific tool may allow for cross comparison between disease groups but also allow the sensitivity to identify the frailty specific nuances associated with that condition. This is akin to the role of questionnaire quality of life assessment.

Such markers of frailty vary considerably and there are inconsistencies with regards to what is measured across the components of frailty including mobility / balance, nutrition and cognitive function. The methodological process that has led to the development of the AVFS and the LAVFS means that multiple domains associated with frailty have been assessed. Comparison between the AVFS and more commonly used generic frailty scores will enhance the validity of the AVFS.

The results presented in this study help fill the current gap in knowledge on the longer-term effects of frailty on patients who are admitted under the care of vascular surgeons.

The exclusion criteria were determined to avoid the inclusion of patients admitted overnight for observation after minor procedures such as angioplasty or varicose vein treatments, as well as to concentrate on frailty as an age-associated decline. This also meant that those patients who died within 48 hrs of admission were excluded. This consisted mainly of patient with a ruptured AAA (n=4), patients with acute limb ischaemia (n=3), one patient with trauma and then 4 other patients with a mixture of presentation. This number is very small and therefore also of little statistical significance. We are happy that the dataset we have used is robust and those data points that did not have complete data were excluded from analysis. The accuracy of the data entered into the patient notes was not validated due to the retrospective nature

but we have no reason to question that accuracy. Further while we identified all readmission to hospitals within our own vascular network, we are unable to determine whether any of this cohort of patients were admitted to hospitals outside our network although we feel that the numbers if any would be small and unlikely to affect the overall results or conclusions. We also need to be wary that in those with CLTI, independent mobility may be limited more by the presenting cause rather than more general comorbidity. Subgroup analysis with regard to admission diagnosis was not possible because the number of patients in each group was too small. It is known that infrainguinal revascularization for severe limb ischaemia contributes to poor postoperative mobility and increased likelihood of discharge to a care facility<sup>27-8</sup>.

In conclusion, this study demonstrates that frailty has significant effects on multiple key outcomes for vascular surgical patients. As the population continues to age, improving our understanding of the relationship between frailty and outcomes in surgical patients is critical as it informs decision making by the clinicians. We believe that future work in the field should focus on continuous re-validation of tools which we use for assessing frailty and using these to identify correctable patients' factors to improve not only short term but longer-term outcomes in vascular surgery patients.

## Disclosures

None.

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## Captions for Figures

Figure 1: Diagrammatic representation of all patients included and excluded in the study.

Figure 2: Cumulative Kaplan-Meier five-year survival estimates stratified by (a) Addenbrookes Vascular Frailty Score (AVFS) and (b) Long-term Addenbrookes Vascular Frailty Score (LAVFS). Patients with scores of 5 or 6 have been combined into a single group as there were very few patients with a score of 6.

Figure 3: Receiver Operator Curve (ROC) curves for Addenbrookes Vascular Frailty Score (AVFS) and long-term AVFS (LAVFS) showing 5-year survival discrimination.

Figure 4: Cumulative Kaplan-Meier five-year readmission-free survival stratified by Addenbrookes Vascular Frailty Score (AVFS). Patients with scores of 5 or 6 have been combined into a single group as there were very few patients with a score of 6.



## Captions for Tables

Table 1: Frailty characteristics of patients assessed with the study. Laboratory measurements such as serum albumin were based on samples taken within 12 hours of admission to hospital. If multiple samples were available, the first was used. All of the remaining items are routinely documented on admission as part of the standard medical and/or nursing proforma in our institution. CCI: Identifies 22 comorbid conditions, and assigns them a score of 1, 2, 3, or 6, depending on the risk of dying associated with each one. Scores are summed to provide a total score. Clinical conditions and associated scores are as follows: 1 each: Myocardial infarct, congestive heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic lung disease, connective tissue disease, ulcer, chronic liver disease, diabetes. 2 each: Hemiplegia, moderate or severe kidney disease, diabetes with end organ damage, tumour, leukaemia, lymphoma. 3 each: Moderate or severe liver disease. 6 each: Malignant tumour, metastasis, AIDS.

Table 2: Predictors of long-term survival on univariate and multivariate analysis. ITU, intensive treatment unit; Hb, haemoglobin. \*Significant at 1-percent level after Bonferroni–Holm correction. †Significant at 5-percent level after Bonferroni–Holm correction. ‡Log rank test. §Wald P-value for predictor; these six significant factors form the Long-term Addenbrooke’s Vascular Frailty Score.

Table 3: Predictors of long-term readmission-free survival on univariate and multivariate analysis. ITU, intensive treatment unit; Hb, haemoglobin. \*Significant at 1-percent level after Bonferroni–Holm correction. ‡Log rank test. §Wald P-value for predictor.

Table 1.

<b>Frailty domain</b>	<b>Characteristic</b>	<b>Definition/Source of data</b>
Comorbidity	Number of medicines on admission	Number of medications documented in the admission clerking
	Charlson comorbidity index (CCI) <sup>29</sup>	Charlson comorbidity index (not including points for age) calculated on admission
	Anaemia	Haemoglobin concentration less than 11.9g/dL
Physical function	Katz score <sup>30</sup>	Katz score calculated on admission. The score looks at 6 aspects of function and defines them as either dependent or independent. The 6 aspects are bathing, dressing, toileting, transferring, continence and feeding. This provides a score from 0 (very dependent) to 6 (independent).
	Pre-admission mobility	Mobility as documented on admission (Mobilises independently, mobilises with walking aids, dependent on others).
Nutrition	Waterlow score <sup>31</sup>	Waterlow score calculated on admission. This is a score to predict risk of a pressure sore. The following areas are assessed for each patient and assigned a point value. Build/weight for height, skin type/visual risk areas, sex and age, malnutrition screening tool, continence and mobility.

	Serum albumin	Serum albumin
	Weight and BMI	Weight (kg) and BMI as documented on admission.
	Evidence of malnutrition	Moderate to high risk of malnutrition assessed using the local screening tool (a modification of the Glasgow Nutritional Screening Tool <sup>32</sup> ).
Cognition	Cognitive impairment	Any documented past medical history of dementia in medical or nursing notes.
	Depression	Any documented past medical history of depression in medical or nursing notes or currently taking antidepressants.
Geriatric syndrome	History of falls	History of two or more falls in the last 12 months.
	Visual impairment	History of visual impairment including refractive defects, visual field defects, and reduced peak contrast sensitivity not corrected by glasses on admission.
	Hearing impairment	History of hearing loss or impairment in either or both ears, need for a hearing aid, or a history of deafness on admission.
Social vulnerability	Living alone	Patient lives alone in an independent residence (patient may have carers coming

		in regularly to help with activities of daily living).
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Table 2.

Predictor	Number with predictor (%)  N=410	Univariate P-value <sup>‡</sup>	Multivariate analysis	
			Hazard ratio (95% C.I.)	P-value <sup>§</sup>
Age $\geq$ 77 on admission	204 (49.8)	<0.001*	1.59 (1.16–2.20)	0.004
Male Sex	289 (70.5)	<0.001*		
Not Independently Mobile On Admission	118 (28.8)	<0.001*	2.34 (1.56–3.52)	<0.001
Lives Alone	176 (42.9)	0.019		
Katz Score < 6	93 (22.7)	<0.001*	0.67 (0.43–1.04)	0.077
Charlson comorbidity index > 2	197 (48.1)	<0.001*	2.10 (1.52–2.91)	<0.001
Depression	24 (5.9)	0.008 <sup>†</sup>		
Went to ITU during admission	37 (9.0)	0.832		
Previous Surgery	313 (76.3)	0.539		
Previous ITU	10 (2.4)	0.688		
Conservative treatment	34 (8.3)	<0.001*		
Limb-related admission	173 (42.2)	<0.001*		

Polypharmacy on admission (> 8 medications)	168 (41.0)	<0.001*	1.70 (1.25–2.31)	<0.001
Visual Impairment	38 (9.3)	<0.001*		
Hearing Impairment	44 (10.7)	0.004†		
Memory Problems	25 (6.1)	<0.001*		
Waterlow on Admission (> 13)	175 (42.7)	<0.001*		
Evidence of Malnutrition	58 (14.2)	<0.001*	1.83 (1.27–2.64)	0.001
Two or more Falls last 12 months	63 (15.4)	<0.001*		
Hb On Admission (< 11.9 g/dL)	203 (49.5)	<0.001*		
Albumin on Admission	-	<0.001*		
Emergency Admission	166 (40.5)	<0.001*	1.86 (1.37–2.51)	<0.001

Table 3.

Predictor	Number with predictor (%)  N=410	Univariate P-value <sup>‡</sup>	Multivariate analysis	
			Hazard ratio (95% C.I.)	P-value <sup>§</sup>
Age $\geq$ 77 on admission	204 (49.8)	<0.001*	1.31 (1.04–1.65)	0.020
Male Sex	289 (70.5)	0.113		
Not Independently Mobile On Admission	118 (28.8)	<0.001*	1.28 (1.00–1.65)	0.052
Lives Alone	176 (42.9)	0.374		
Katz Score < 6	93 (22.7)	<0.001*		
Charlson comorbidity index (>2)	197 (48.1)	<0.001*	1.37 (1.08–1.73)	0.052
Depression	24 (5.9)	0.181		
Went to ITU during admission	37 (9.0)	0.452		
Previous Surgery	313 (76.3)	0.535		
Previous ITU	10 (2.4)	0.402		
Conservative treatment	34 (8.3)	0.019		
Limb-related admission	173 (42.2)	<0.001*	1.27 (1.00–1.63)	0.054

Polypharmacy on admission (> 8 medications)	168 (41.0)	<0.001*	1.34 (1.06–1.68)	0.014
Visual Impairment	38 (9.3)	0.314		
Hearing Impairment	44 (10.7)	0.050		
Memory Problems	25 (6.1)	0.187		
Waterlow on Admission (> 13)	175 (42.7)	<0.001*		
Evidence of Malnutrition	58 (14.2)	0.020		
Two or more Falls last 12 months	63 (15.4)	<0.001*		
Hb On Admission (< 11.9 g/dL)	203 (49.5)	0.113		
Albumin on Admission	-	0.450		
Emergency Admission	166 (40.5)	<0.001*	1.46 (1.16–1.83)	0.001